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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,074	09/25/2003	Kenneth W. Dobie	AMGN0001-101 (A-829A)	8427

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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,074	DOBIE ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 19-41* is/are pending in the application.

4a) Of the above claim(s) *30-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 19-29* is/are rejected.

7)☒ Claim(s) *14 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/4/04, 3/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 30-41are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/20/05.

Applicant's traverse the restriction requirement state is it not a burden to search more than one sequence in claims 14-15 because all the sequences are "structurally similar (e.g. they are oligomeric compounds)" and further they are all "functionally similar (e.g. all inhibit forkhead box O1A)."

While it is true that all the sequences are oligomeric compounds that are targeted to forkhead box O1A, each sequence is considered to be unrelated since each sequence claimed is structurally independent as evidenced by each unique sequence, as stated in the previous Restriction requirement filed 10/24/2005. As such, due to the complex nature of the search and corresponding examination of more than one of the claimed sequence, restriction is proper because a search for one sequence would not necessarily reveal art against the other sequences.

Applicant further argues restriction between the methods of groups II, III and IV is not proper because the methods are related in that they all function to decrease forkhead box O1A expression. As stated in the previous office action, the method of group II is drawn to decreasing forkhead box O1A in cells or tissues, which is materially different than a method for screening for putative compound inhibitors as present in group III and is materially different than the method of decreasing blood or plasma glucose levels, improving glucose tolerance or regulating

insulin levels as present in group IV. Furthermore, the methods of groups II, III and IV require steps that are not capable of use together and therefore restriction is proper and made FINAL.

Status of the Application

Claims 1-15 and 19-41 are pending. Claims 1-15 and 19-29 are currently under examination. Claims 30-41 are withdrawn as being drawn to a non-elected invention.

Claim Objections

Claims 14 and 15 are objected to as being dependent upon a rejected base claim and reciting non-elected subject matter, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

Claim Rejections - 35 USC § 102 or 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 10-13 and 19 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Barr et al. (U.S. Patent No. 5,650,278).

The instant claims are drawn to a compound 8 to 80 nucleobases in length targeted to a nucleic acid encoding forkhead box O1A wherein the compound is at least 70% complementary to said nucleic acid molecule, wherein the forkhead box O1A is human or mouse and wherein the compound modulates expression by at least 70%, 80%, 90% or 95%.

Barr et al. teach an oligonucleotide (SEQ ID NO. 14, Result 30 in database .rni sequence search), 20 nucleobases in length, targeted to a nucleic acid encoding a human forkhead box O1A (nucleobases 1241-1260) and a mouse human forkhead box O1A (nucleobases 1275-1294) wherein the compound is 100% complementary to the nucleic acid encoding a human forkhead box O1A or 90% complementary to a nucleic acid encoding a mouse human forkhead box O1A. Thus, the nucleic acid sequence taught by Barr et al. meets the structural limitation of claims 1-3, 10-13 and 19 of the instant application. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Therefore, the instant claims are anticipated or obvious over Barr et al.

Claims 1-2, 4-13 and 19-22, 24, 27 and 29 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Cook et al. (U.S. Patent No. 5,576,302).

The instant claims are drawn to a compound 8 to 80 nucleobases in length targeted to a nucleic acid encoding forkhead box O1A wherein the compound is at least 70% complementary to said nucleic acid molecule, wherein the forkhead box O1A is human, wherein the compound is targeted to the 5' untranslated, start codon, stop codon or 3' untranslated regions, wherein the compound modulates expression by at least 70%, 80%, 90% or 95%, wherein the compound comprises an antisense oligonucleotide, wherein the compound has at least one modified phosphorothioate, internucleoside linkage, sugar moiety or nucleobases modification and further drawn to a composition comprising a pharmaceutically acceptable carrier or diluent.

Cook et al. teach an antisense oligonucleotide, 19 nucleotides in length, targeted to a nucleic acid encoding a human forkhead box O1A (SEQ ID NO. 12, result 72 in database .rni sequence search) wherein the compound is 95 % complementary to the target. Cook et al. further teach the antisense compound has at least one modified phosphorothioate, internucleoside linkage, and sugar moiety or nucleobases modification. Cook et al. further teach a composition comprising said antisense compound and a pharmaceutically acceptable carrier or diluent.

Thus, the compound taught by Cook et al. meets the structural limitation of claims 1-2, 4-13 and 19-22, 24, 27 and 29 of the instant application. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C.

102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Therefore, the instant claims are anticipated or obvious over Cook et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 4-15 and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (U.S. Patent No. 5,576,302) in view of Baracchini et al. (U.S. Patent No. 5,801,154) and Bennett et al. (U.S. Patent No. 5,998,148).

The instant claims are drawn to a compound 8 to 80 nucleobases in length targeted to a nucleic acid encoding forkhead box O1A wherein the compound is at least 70% complementary to said nucleic acid molecule, wherein the forkhead box O1A is human, wherein the compound comprises an antisense oligonucleotide, wherein the antisense is targeted to the 5' untranslated, start codon, stop codon or 3' untranslated regions, wherein the compound has at least one modified phosphorothioate, internucleoside linkage, 2'-O-methoxyethyl sugar moiety or 5-

methylcytosine nucleobases modification and further drawn to a composition comprising a pharmaceutically acceptable carrier or diluent.

Cook et al. teach an antisense oligonucleotide, 19 nucleotides in length, targeted to a nucleic acid encoding a human forkhead box O1A (SEQ ID NO. 12, result 72 in database .rni sequence search) wherein the compound is 95 % complementary to the target. Cook et al. further teach the antisense compound has at least one modified phosphorothioate, internucleoside linkage, and sugar moiety or nucleobases modification. Cook et al. further teach a composition comprising said antisense compound and a pharmaceutically acceptable carrier or diluent. Cook et al. does not teach antisense sequences or chimeric oligonucleotides targeted to the 5' untranslated, start codon, stop codon or 3' untranslated regions wherein the antisense compound comprises 2'-O-methoxyethyl sugar moiety or 5-methylcytosine nucleobase modifications and further does not teach a composition comprising an antisense sequence and a colloidal dispersion system.

Baracchini et al. teach that antisense oligonucleotides can be used for research purposes, and also teach that preferred antisense oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition (see Column 6). Baracchini et al. teaches that such modifications are desirable in antisense oligos because these modifications have desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. Baracchini et al. provide specific embodiments of such modifications at columns 6-8 and in Example 1. These specific examples taught by Baracchini et al. include the presently claimed phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and chimeric oligonucleotides. Tables 1-4 show the successful design

and use of modified oligonucleotides in cells in culture. Table 1 exemplifies the successful practice of general antisense design taught at columns 8-10. Baracchini et al. also teaches at column 8 that antisense oligonucleotides are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length and further teach in column 9 preferred targeting the 5' untranslated, start codon, stop codon or 3' untranslated regions. Baracchini et al. is considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

The teachings of Bennett et al. are considered to parallel those of Baracchini et al. Column 5 indicates that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. Columns 6-7 teach that preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, among others. Columns 7-8 teach that preferred antisense oligonucleotides comprise modified sugar moieties including 2'-O-methoxyethyl and teach preferred targeting of said compound to specific regions of the target gene, namely the 5' UTR, start, coding, stop or a 3'-untranslated regions (see Columns 3-4). Bennett et al. also teach one of ordinary skill to modify nucleobases in antisense oligonucleotides, including the teaching of 5-methylcytosine (see Column 8-9), and also to use chimeric antisense oligonucleotides (see Column 9-10). Bennett et al. also teach antisense compounds can be utilized in kits or diagnostic assays (see Column 12) and further teach compositions comprising colloidal dispersion systems (see Column 14). Bennett et al. teach that the above modifications are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. Table 1 teaches the successful targeting of those regions taught in columns 3-4 with chimeric

phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification). Thus, Bennett et al. is also considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

It would have been obvious to one of ordinary skill in the art to incorporate modifications as taught by Baracchini et al. and Bennett et al. into said antisense compound, as taught by Cook et al.

One would have been motivated to modify said antisense compound, as taught by Baracchini et al. and Bennett et al., because both teach that such modifications increase an antisense compound's cellular uptake, target affinity and resistance to degradation which are all desirable properties of therapeutic antisense compounds.

Finally, one would have a reasonable expectation of success given that Baracchini et al. and Bennett et al. both teach making modified antisense compounds targeted to distinct regions of a target gene, the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

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Kimberly Chong
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1635